Remarks

Reconsideration of this Application is respectfully requested.

Claims 61-120 are pending in the application, with claims 61 and 90 being the independent claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 102(e)

For rejections under 35 U.S.C. § 102, the Federal Circuit held "[a] claim is anticipated only if *each and every element* as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California,* 814 F.2d 628, 613, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (emphasis added).

Vande Woude *et al.*

Claims 61-64, 66-70, 77-83, 87-93, 95-99, 106-112, 116-120 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Vande Woude *et al.* (U.S. Pat. No. 5,645,988). The Examiner alleged that Vande Woude *et al.* teaches a parallel screening method for determining the pharmacological effects of an anti-cancer drug on the activity of different biological target molecules contained in cancer cells of the same type comprising the steps of the instant claims. Applicants respectfully traverse this rejection.

Vande Woude *et al.* does not describe the parallel screening of the instant claims, which is defined in the instant specification, *inter alia*, on page 6, lines 11-17, as a high throughput screen in which several substances "are applied in parallel to one or more sets of cellular substrates, each set constituting a group of different assays or assay formats based on the same starting cell." One embodiment of this parallel screen is described in Example 1(g) "Comparative screening and testing for specificity", beginning on page 41 of the instant specification, in which dilutions of the test substances were added in parallel to several cell lines, incubated and cell number determined.

In contrast, the assay only very generally described in Vande Woude *et al.* makes no mention of a parallel screen, as illustrated by the following representative description:

> [A] method of identifying a drug which selectively inhibits the growth of a particular type of cancer cell, which method comprises (a) contacting with the drug at least two cancer cells derived from the same type of biological material, wherein the cancer cells differ as to the presence of a particular DNA sequence, (b) measuring the effect of the drug on the growth of the cancer cells, and (c) determining whether there is a correlation between the effect of the drug on the cancer cells and the presence or absence of the DNA sequence in the cancer cells.

Column 5, lines 40-50. This description fails to teach a combination of multiple assays into one step for a high throughput parallel screen. The assay of Vande Woude *et al.* is further described in columns 11 and 12, but does not describe or suggest a parallel screen, nor do the Examples. The support in Vande Woude *et al.* the Examiner cited in the rejection does not teach a parallel screen. There is nothing in Vande Woude *et al.* to

support the conclusion that a parallel screen was a feature of that assay. Because Vande Woude *et al.* does not teach each and every limitation of the rejected claims, it cannot anticipate the claims. Applicants respectfully request that the rejection be withdrawn.

The Examiner also rejected claim 90 and dependents thereof over the assay described in Vande Woude *et al.* In addition to the arguments presented *supra*, Applicants point out that claim 90 and its dependents are drawn to a parallel screening assay utilizing *different cell types* containing the *same target molecule.* Since Vande Woude *et al.* only discloses an assay utilizing cells of the same type, but different target molecules (*see e.g.*, column 5, lines 40-50 and the Examiner's description on page 3 of the outstanding Office Action), it cannot anticipate claims 90 and its dependents. Applicants respectfully request that the rejection be withdrawn.

Tang *et al.*

The Examiner rejected claims 61, 62, 67-73, 77-79, 90, 91, 96-102, 106-108 under 35 U.S.C. § 102(e) as allegedly being anticipated by Tang *et al.* (U.S. Pat. No. 5,710,173). Specifically, the Examiner alleged that "Tang *et al.* teach a parallel screening method (96-well microtiter plates) of claims 61-62, 90-91, of determining the pharmacological effect of a substance (anti-cancer drug) on the activity of different biological target molecules contained in test cells of same type . . ." Page 5 of the Office Action. Applicants respectfully traverse this rejection.

Tang *et al.* does not describe the parallel screening method of the claimed invention, which is explained in detail *supra*. The Examiner apparently points to the 96 well format of the endpoint ELISA assay described in the Group II ELISA Type Assay

Examples beginning in column 18 of Tang *et al.* as support for a parallel screen. However, there is no mention whatsoever of performing sets of different assays *in parallel*. Indeed, Tang *et al.* suggests they are performed sequentially.

> Compounds of varying degree of selectivity are useful for diagnosing the role of a receptor tyrosine kinase. For example, compounds which inhibit more than one type of receptor tyrosine kinase can be used as an initial test compound to determine if one of several receptor tyrosine kinases drive the disorder. More selective compounds can then be used to further eliminate the possible role of different receptor tyrosine kinases in driving the disorder.

Column 11, lines 4-11. The Examples describe each assay individually and do not make any reference to combining the assays into a single step. Mere use of the well-known 96 well ELISA format is not sufficient for describing a parallel screening assay according to the claimed invention. The 96 well format is typically used for the processing of multiple samples of the *same* ELISA assay, and nothing in Tang *et al.* teaches otherwise. Indeed, it appears that the multiple samples come from the same cells that are treated with different drugs as a part of a serial screen. These ELISA samples within each Example are not described as coming from either cells of the same type containing different biological target molecules, or cells of different types containing the same target molecule. There is no description of performing different assays or assay formats within a parallel screening step. Performing the same assay multiple times is not a parallel screen utilizing "a number of different assays or assay formats" as described on page 4, lines 4-8 of the instant specification. Because Tang *et al.* does not describe a

parallel screening method, it does not teach each and every element of the instant. Therefore, Tang *et al.* cannot anticipate the claimed invention, and Applicants respectfully request that the rejection be withdrawn.

The Examiner also rejected claim 90 and dependents thereof over the assay described in Tang *et al.* In addition to the arguments presented *supra*, Applicants point out that claim 90 and its dependents are drawn to a parallel screening assay utilizing *different cell types* containing the *same target molecule*. Since Tang *et al.* only discloses an assay utilizing cells of the same type, but different target molecules (*see e.g.*, the Group II ELISA Type Assay Examples and the Examiner's description on page 5 of the outstanding Office Action), it cannot anticipate claims 90 and its dependents. Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. § 103

In re Vaeck (947F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)), outlines the factors required for establishing a prima facie case for obviousness: prior art references that teach all claim limitations, a motivation to combine the references in the references themselves or knowledge known to a person of skill in the art at the time the invention was made, and a reasonable expectation of success from the combination elements in the references. As discussed below, Applicants respectfully assert that these requirements have not been met to support a *prima facie* argument for obviousness for the instant claims.

Vande Woude *et al.* in view of Czernilofsky *et al.*

Claims 74-76, 84, 85, 103-105, 113, and 114 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Vande Woude *et al.* in view of Czernilofsky *et al.* (U.S. Pat. No. 5,854,004). Specifically, the Examiner alleges that the claims are obvious over the parallel screen allegedly disclosed in Vande Woude *et al.* and the additional target molecules and detection systems allegedly disclosed in Czernilofsky *et al.* Applicants respectfully traverse this rejection.

As discussed *supra*. Vande Woude *et al.* does not teach the parallel screen of the instant claims. Czernilofsky *et al.* does not remedy this deficiency. In column 6, lines 30 -35, Czernilofsky *et al.* state that the method serves to screen substances that modulate a phospholipase C signal transduction pathway depending on an individual receptor. The screening method of Czernilofsky *et al.* has the purpose to identify a test substance with the ability to modulate, in one type of cell, a signal transduction pathway of interest which is dependent on a specific receptor molecule of interest.

When mentioning, in column 7, lines 62 - 67, that parallel tests may be carried out, Czernilofsky *et al.* do not refer to a parallel screening method of the instant claims. The use of cells that contain a sensor DNA responding to a different signaling pathway and that may (CRE-test cells) or may not (CRE-pretest cells) contain the receptor of interest in parallel to the actual test cells merely serves the purpose of specificity control with regard to the predetermined signal transduction pathway of interest.

In order to make sure that the compound's modulating effect is specific with regard to the receptor, further control tests may be carried out by using cells that contain

other different receptors (column 13, lines 66 -68). The very use of the term "further" points out that these tests are not conducted in parallel, but may be carried out in addition., *i.e.* after a compound has already been identified. Such tests do not aim at identifying compounds that act on different receptors (targets). On the contrary, they have the purpose, by serving as controls, to exclude compounds that are not specific for the receptor of interest in that they also influence one or more other receptors.

There is no motivation to combine the sophisticated receptor-mediated assay of Czernilofsky *et al.* with the simple proliferation assay based on the effect of oncogenes and tumor suppressor genes of Vande Woude *et al.* Vande Woude *et al.* is in the field of cancer and oncogenes, while Czernilofsky *et al.* is directed to receptor-mediated intracellular signaling. Neither reference suggest the desirability of their assay for the other field.

Further, there would be no expectation of success without impermissible hindsight as Vande Woude *et al.* does not describe the regulatory elements of the genes assayed therein that would be required for the "sensor" DNA of the assay of Czernilofsky *et al.* Without these regulatory elements, it is impossible to adapt the signalling responsiveness of Czernilofsky *et al.* to the oncogene screen of Vande Woude *et al.* Therefore, because the combination of references do not teach each and every element of the claims, contain any suggestion to combine, or have any expectation of success without impermissible hindsight, Applicants assert that the Examiner has not met the burden for a *prima facie* case for obviousness. Applicants respectfully request that the rejection be withdrawn.

Vande Woude *et al.* in view of Czernilofsky *et al.* in further view of Chalfie *et al.*

Claims 86 and 115 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Vande Woude *et al.* in view of Czernilofsky et al in further view of Chalfie *et al.* Specifically, the Examiner asserted that the alleged parallel screen of Vande Woude *et al.*, the reporter genes and target receptors of Czernilofsky *et al.*, and the green fluorescent protein (GFP) of Chalfie *et al.* render the instant claims obvious. Applicants respectfully traverse this rejection.

Vande Woude *et al.* and Czernilofsky *et al.* have been discussed *supra*. Chalfie *et al.* does not remedy their deficiencies as it merely teaches the use of GFP as a reporter gene. It does not teach the parallel screen of the instant claims or remedy any of the specific deficiencies discussed of Vande Woude *et al.* or Czernilofsky *et al.* Therefore, since this combination of references do not teach each and every element of the claims, contain any suggestion to combine, or have any expectation of success without impermissible hindsight, Applicants assert that the Examiner has not met the burden for a *prima facie* case for obviousness. Applicants respectfully request that the rejection be withdrawn.

Vande Woude *et al.* in view of Reed *et al.*

Claims 65 and 94 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Vande Woude *et al.* in view of Reed *et al.* Specifically, the Examiner asserted that the alleged parallel screen of Vande Woude *et al.* combined with the BAP and Bcl-2-related solid-phase protein binding assays of Reed *et al.* Applicants respectfully traverse this rejection.

Vande Woude *et al.* does not describe the parallel screen of the instant claims, as described *supra*. Reed *et al.* does not remedy this deficiency as the screen described therein is a binding assay of proteins fixed to a solid support (*see* Figure 7 and Example VII). It does not describe the parallel screen of applying test substances on test cells containing biological target molecules and measuring the effect the substance has on the biological activities selected from metabolic-coupled signal transduction, receptor-couples transduction, or pathological effects. The assay of Reed *et al.* only measures binding affinities of the test substances to certain proteins and cannot measure the biological effects of the test substances. Therefore, since the combination of Vande Woude *et al.* and Reed *et al.* do not teach each and every element of the claims, contain any suggestion to combine, or have any expectation of success without impermissible hindsight, Applicants assert that the Examiner has not met the burden for a *prima facie* case for obviousness. Applicants respectfully request that the rejection be withdrawn

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

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